P204 Ageing and Adrenomedullin in the Female Reproductive System of the Rat

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Objective: To investigate the age-related changes in the gene expression of adrenomedullin (AM), its receptor (CRLR, calcitonin receptor-like receptor) and its receptor activity modifying proteins (RAMPs) and coupling protein (RCP) in the ovary, oviduct and uterus of female rats aged 3 months (young) and 20 months (old) at oestrus and dioestrus. **Methods:** The stages of the oestrus cycle were determined by vaginal smear. AM levels in the plasma, the ovary, the oviduct and the uterus were assayed by RIA while the mRNA levels were measured by RT-PCR. **Results:** The young rats were cycling while the old rats were in either constant oestrus or constant dioestrus. In the young rats, the plasma AM levels were higher at dioestrus than at oestrus. In the ovary of the young rat, the preproAM mRNA and AM levels were higher at dioestrus than at oestrus. Plasma AM levels were lower in the old rats than in the young rats. There were age-related decreases in AM levels at both dioestrus and oestrus in the oviduct, but only at dioestrus in the ovary and the uterus. Both preproAM mRNA and CRLR mRNA levels decreased in the ovary, oviduct and uterus of the old rats at oestrus as well as at dioestrus. In the ovary of the old rats, RAMP2 mRNA decreased at both stages. In the oviduct, mRNA levels of all RAMPs decreased at both stages. In the uterus, RAMP3 decreased at both stages while RAMP1 and RAMP2 mRNA levels decreased only at oestrus. The mRNA levels of RCP decreased in the old rats in all three tissues at both stages. **Conclusion:** These results demonstrate that ageing has similar effects on the levels of AM and its receptor component proteins in the ovary, the oviduct and the uterus. The decrease in AM actions in the female reproductive systems may contribute to the decline of reproductive function in the ageing female rat.

P205 Effect of MEN1 on Development of Embryonic Development In Vitro and Differences in Gene Expression between men1+/+ and men1 -/-l Knockout Embryonic Stem Cells

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The MEN1 gene has been identified as the gene responsible for MEN1, a hereditary syndrome transmitted with an autosomal dominant trait. In the other's study generation of mice with a null-mutation in the men1 gene revealed a crucial role in embryonic development. In this study, we used embryoid bodies (EBs) formed from men1+/+ and men1 -/- ES cells as a model system to investigate effect of on the embryo development, which recapitulated some features of early embryogenesis in vitro. Morphological analysis showed that EBs formed by the men1 -/-l ES cells were much similar in size and number to those formed by men1+/+ ES cells during the 10 days of suspension culture. We propose proliferation capacity of ES cells seem not to be impaired in the absence of menin. We also studied on differences in gene expression between men1+/+ and men1 -/-l knockout embryonic stem cells utilizing Affymetrix chips. 115 of these genes were increased and 565 were decreased by at least 2-fold in the men-/- ES relative to men+/+ including genes involved in TGFβ Signaling Pathway (e.g. smad3, smad1, Thbs1, Zfhx1b, Runx2, Inhba), Wnt signaling Pathway (e.g. Wnt5a), G Protein Signaling Pathway (e.g. Gna13, Akap9) and genes involved in Apoptosis (e.g. Traf3, Dffb, Jun, Mdm2, Irf2). We have identified a number of putative men1 target gene such as: Thbs1, Runx2, Wnt5a, etc. More experiments are needed.